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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's arguments have been respectfully reconsidered but have not been found persuasive.

Claims 1, 3, 5, 6, 11, 12, 23 and 24 are pending. Claims 7, 9, 10, 20 and 22 have been cancelled and claims 11 and 24 have been amended by Applicants' amendment filed on 12-22-2009.

Filing of a pre-appeal brief request for review on 12-23-2009 is acknowledged.

Withdrawn Objections/Rejections in response to Applicants' arguments or amendments

Claim Objection

In view of Applicants' amendment of claim 24 to spell out the abbreviation, "TA-MUC1", objection to claim 24 has been withdrawn.

Claim Rejections - 35 USC § 112-Enablement

In view of Applicants' cancelation of claims 20 and 22, rejection of claims 20 and 22 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is rendered moot.

In view of the withdrawn rejection, applicant's arguments are rendered moot.

Objections/rejections maintained in response to Applicants' arguments or amendments

Claim Rejections - 35 USC § 102

Claim 1 remains rejected under 35 U.S.C. §102(b) as being anticipated by Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of

record) as evidenced by Benoist et al., (1992, Immunology Letters, pp. 45-55) and Karsten et al., (1998, Cancer Research pp. 2541-2549, of record).

Applicants have not submitted new arguments to rebut rejection of Claim 1 under 35 USC § 102 made in the Office Action filed on 10-07-2009. Therefore, claim 1 remains rejected under 35 USC 102 for the reasons already of record.

The response to Applicants' Arguments filed on 09-23-2009 as it applies to rejection of claims 1, 5, 6, 11, 12 and 24 under 35 USC 103 in the paragraphs below is essentially reiterated as it was argued and set forth at pages 6 and 7 of the office action filed on 10-07-2009

At page 9-10 of the remarks filed on 09-23-2009, Applicants essentially argue that: 1) the Examiner believe that TF is necessarily present in the MUC-1 transformed K562-derived cells of *Ichiyama*, 2) the examiner appears to believe against the disclosure at page 6 of the specification stating that, "TF corresponds to exposed core-1 (Galβ1-3GalNAc)" that any carbohydrate structure that contains a core-1 unit "expresses TF". Applicants' arguments have been fully considered but they are not persuasive.

Regarding 1) and 2), the examiner believes that lack of detection of TF in a binding assay is not evidence that the TF antigen (glycotope) (Galβ1-3GalNAcα-O-Ser/Thr (Core 1)) is not expressed in the MUCl-transformed K562 cells of Ichiyama which are transfected with the full length cDNA MUC1 molecule. Applicants appear to equate expression on the cell surface of the TF antigen with an "exposed TF antigen". Indeed, prior art filed by the inventors in the IDS of 04-27-2009, defines ,"TF is the disaccharide Galβ1-3GalNAc which is O-glycosidically linked in an α-anomeric configuration to the hydroxy amino acids serine or threonine or proteins) (Galβ1-

3GalNAcα-O-Ser/Thr" and "TF equals the core-1 structure of O-linked carbohydrate chains which where originally described as mucin-type glycans" (Goletz et al., Advances in Experimental Medicine and Biology, 2003, pp:147-62; page 148). Furthermore, Goletz et al., (2003) states, "the innermost core-sugar of O-glycan chains is also called Tn when exposed in carcinomas. Tn is the substrate for further glycosyltransferases leading to di- or trisaccharides which represent the O-glycan core structures Core-1 to Core-6… The Core-1 (TF) is generated by the activity of UDP-Gal:GalNAc-R-β-galactosyl-transferase" (age 149, paragraphs 1 and 2). Indeed, Figure 1 in the specification evidences that wild type K562 cells before magnetic separation express TF, Tn, GPA, AGPA and MUC1 markers. What applicants have obtained with enzymatic desialylation with neuramidase treatment is an enriched population K562-derived cell for TF, i.e., NM-F9 and NM-D4.

Claim Rejections - 35 USC § 103

Claims 1, 5, 6, 11, 12 and **24** remain rejected under 35 USC 103 as being unpatentable over Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of record) as evidenced by Hinoda (2005, Journal of Clinical Laboratory Analysis, pages 100 – 104, Abstract), in view of Benoist et al., (Immunology Letters 1992, pp. 45-55) and Karsten et al., (1998, Cancer Research pp. 2541-2549, of record) and further in view of Horton et al., (U.S. Patent 7,268,120, Date of filing Apr. 21 2000).

Applicants have not submitted new arguments to rebut rejection of 1, 5, 6, 11, 12 and 24 under 35 USC § 103 made in the Office Action filed on 10-07-2009. Therefore, claims 1, 5, 6, 11, 12 and 24 remain rejected under 35 USC 103 for the reasons of record.

The response to Applicants' Arguments filed on 09-23-2009 as it applies to rejection of claims 1, 5, 6, 11, 12 and 24 under 35 USC 103 in the paragraphs below is

essentially reiterated as it was argued and set forth at pages 7-10 of the office action filed on 10-07-2009

At pages 10 and 11, Applicants essentially argue: 1) that Ichiyama neither alone or in combination with Hinoda, Benoist, Karsten and Horton teaches or suggests cells that express TF antigen on the cell surface, 2) Karsten discloses cell free MUCl-derived glycopeptides engineered to contain TF, 3) Karsten's report of synthetic TF-containing peptides offers no teaching or suggestion of a cell line that expresses TF on its surface, which requires the cell's own synthesis machinery to produce the antigen, 4) Horton's erroneously suggest that TF is an immunogenic polypeptide, 5) "Horton's mere recitation of the term TF is without probative value--a characterization unrebutted by the Office. See also page 20 of the last Response", and 6) Applicants argue that the claimed cells exhibit unexpected and beneficial properties because the core-1 motif in K562 cells is masked by terminal sialic acids and is therefore unable to elicit an immune response to TF. Applicants' arguments have been fully considered but they are not persuasive.

Regarding 1), the examiner refers applicants to the reasons of record and the reasons set forth in the paragraph above in relation to how the disclosure of Ichiyama obviates the instant invention.

Regarding 2) and 3), Benoist teaches that the K562 tumor cells present glycophorin A (GPA) on the cell surface. Indeed, Benoist discloses that increase of GPA expression on the cell surface may correlate with the resistance of K562 to NK cells (Abstract). Karsten complements the teachings of Ichiyama and Benoist by disclosing the presence of the TF antigen (Galβ1-3GalNAcα-O-Ser/Thr (Core 1)) at multiple positions within the immunodominat region of the MUC1 repeat. Note that Ichiyama discloses

detection of MUC1 with the monoclonal antibody (MAb) MUSE11 which recognizes the continuous amino acid sequence PDTRPAPG as evidenced by Hinoda. The examiner believes this is the same sequence recognized by the TA-specific antibody and identified in the specification as filed at page 7, lies 5-10, as a tumor-associated MUC1 epitope, i.e. TA-MUC1. The TA-MUC1 is commonly known in the art and differs from normal MUC1 by modified glycan side chains, absent evidence to the contrary.

Regarding 4) and 5), Horton complements the teachings of Ichiyama, Benoist and Karsten by disclosing that prior art that teaches that it is routine or well-established in the art to employ *ex vivo* polynucleotide constructs and selective transfection of malignant cells containing polynucleotides expressing therapeutic or prophylactic molecules. Accordingly, if a vector encoding at least a polypeptide of interest including cytokines or immunogenic antigens, e.g., TF and MUC1 can transform and effectively be expressed *ex vivo* cancer cells to induce anti-tumor effector cells, transformation of K562 cells (human erythroleucosis cell stock) with a gene encoding at least a cytokine or MHC I should be reasonably expected to transform and express a target gene in K562 cells for the same reason transfection of *ex vivo* cell or *ex vivo* cell material expresses a DNA encoding a gene target of interest- the inside machinery for transfection and expression on the cell surface of K562 and malignant cells is the same.

Regarding 6), with respect to applicants' argument that, " Applicants submit that the K562-derived cells of Ichiyama would not exhibit this supposedly inherent feature since, as the Examiner has acknowledged, the core-1 motif in K562 cells is obscured by terminal sialic acids and is therefore unable to elicit an immune response. Accordingly, these cells would not be able to generate an immune response to TF, let alone the

surprising and desirable IgG response" is not found persuasive because it is noted that the features upon which applicant relies (i.e., the inner core-1, which equals TF when exposed" according to the instant specification at page 6, lines 9-10) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is the case here. The claims do not recite the carbon substrate characteristics taught in the specification. Hence the argument is not persuasive as they argue limitations that are not present in the claims.

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Claims 1 and 23 remain rejected under 35 USC 103 as being unpatentable over Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of record) in view of Benoist et al., (Immunology Letters 1992, pp. 45-55) and Karsten et al., (1998, Cancer Research pp. 2541-2549, of record), and further in view of Springer G (1997, J Mol Med, pp. 594-602, of record).

Applicants have not submitted new arguments to rebut rejection of 1 and 23 under 35 USC § 103 made in the Office Action filed on 10-07-2009. Therefore, claims 1 and 23 remain rejected under 35 USC 103 for the reasons of record.

Therefore, the rejection of claims 1, 3, 5, 6, 11, 12, 23 and 24 as stated in the previous office action mailed on 10-07-2009 are maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maria Leavitt/

Maria Leavitt
Primary Examiner, Art Unit 1633